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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/204,865	12/03/98	CHEN	J 9584-006-999

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EXAMINER	
LU,F	
ART UNIT	**PAPER NUMBER**
1655	14

DATE MAILED: 02/01/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/204,865	Chen et al.,
Examiner	**Group Art Unit**
Frank Lu	1655

☒ Responsive to communication(s) filed on *9/8/2000 and 11/17/2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11, 13-15, 21-36, 40, 41, 50-52, 58-60, and 62-67* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11, 13-15, 21-36, 40, 41, 50-52, 58-60, and 62-67* is/are rejected.

☒ Claim(s) *4 and 28* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *11*

☒ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. The examiner noticed that claims 57 and 61 have been canceled. Claims 1-11, 13-15, 21-36, 40, 41, 44, 50-52, 58-60, and 62-67 will be examined.

Drawings

2. The drawings submitted on September 8, 2000 have been approved by the office.

Claim Objections

3. Claim 4 and 28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Note that claim 4 and 28 are dependent on claim 1. However, the three-dimensional porous substrate of claim 1 has about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide while said three-dimensional porous substrate of claim 4 or 28 has about 2×10^{-19} to 2×10^{-15} nmol/nm^2 of a capture polynucleotide.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 2-10, 13-15, 21, 22, 24-36, 40, 41, 44, 59, and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claims 2-10, 13-15, 21, 22, 24-36, 40, 41, 44, and 63 are dependent on claim 59.

5. Claim 59 is rejected as vague and indefinite over the phrase "substantially irreversibly" because it is unclear what it intended. Does this phrase mean the binding of capture polynucleotide to a three-dimensional porous substrate is irreversible or this phrase mean something else?

6. The term "high density or high molecular weight" in claims 10, 34, and 67 is a relative term which renders the claim indefinite. The term "high density or high molecular weight" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

7. The term "high stringency or low stringency or moderate stringency" in claims 24, 25 and 36 is a relative term which renders the claim indefinite. The term "high stringency or low stringency or moderate stringency" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Response to Arguments

In page 5, last paragraph bridging to page 6, second paragraph, applicant argued that the expression "high density or ultra-high molecular weight polyethylene" and " high stringency or low stringency or moderate stringency" were "terms well known to one of ordinary skill in the art" and met the legal standard.

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although applicant provided the references to support his position, these references were not found in the specification and were not incorporated by references; Second, note the specification does not give definitions for "high density or ultra-high molecular weight polyethylene" and " high stringency or low stringency or moderate stringency" . High, moderate and low are relative terms, one of ordinary skill in the art can interpret these term based on his/her requirement.

Claim Rejections - 35 U.S.C. § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 60, and 64 are rejected under 35 U.S.C. 102(e) as being anticipated by Beattie (US Patent No. 5,843,767, filed on April 10, 1996).

Beattie teaches microfabricated, flow through porous apparatus for discrete detection of binding reactions.

Regarding to claims 1-5, 8, 9, 14, 15, 21-23, 27-29, 32, 40, 41, 60, and 64, Beattie teaches to tether DNA targets or probes for hybridization using nanochannel glass (NCG) wafers. NCG materials were unique glass structures containing a regular geometric array of parallel holes or channels as small as 33 nm in diameter or as large as several micrometers in diameter. These nanochannel glass structures can possess packing densities in excess of 3×10^{10} channels per square centimeter, fabricated in various array configurations (column 9, eight paragraph). A variety of materials can be immobilized or fixed to the glass surfaces within the channels (housing as

described in claims 21 and 22) of the NCG array, to yield a high surface area to volume ratio. Once the fabrication process was complete, the NCG material was wafered perpendicular to the direction of the channels with a diamond saw and then polished to produce 0.1-1.0 mm sections of material (0.1-1 mm thick) (column 10, second paragraph). For DNA binding capacity, the amount of attaching labeled oligonucleotide to flat glass and gold surface were up to 10^8 probe in a 50 μm and 50 μm area ($4x10^{12}$ probes per square centimeter) (see column 17, third paragraph). Note that the three-dimensional porous substrate of claim 1 has about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide which are equal to about 3.6×10^{12} to 3.6×10^{13} probes per square centimeter. 5' or 3' terminal residue of said capture polynucleotide could be attached to the porous substrate via a linker (column 16, second and third paragraphs). In hybridization reaction, the target DNA sample was flowed into the porous regions of the chip (column 17, fifth paragraph) and hybridized to the nanoporous wafers bearing oligonucleotide probes. Radioactive tags (^{32}P and ^{33}P, incorporated by random priming and PCR reaction) are also used in these experiments (column 18, first paragraph).

Regarding to claims 13 and 60, although Beattie did not describe a three-dimensional porous substrate wherein a porosity was in the range of about 25% to 80%, Beattie did described that the target DNA sample was flowed into the porous regions of the chip (column 17, fifth paragraph) and hybridized to the nanoporous wafers bearing oligonucleotide probes (column 18, first paragraph). This limitation is considered as inherent to the reference taught by Beattie.

Note that, although Beattie did not describe the limitation in claims 24, 25, and 36, the rejections were be made in view of the ambiguity of claims 24, 25, and 36.

Therefore, Beattie teaches the limitations of claims 1-5, 8, 9, 13-15, 21-25, 27-29, 32, 33, 36, 40, 41, 44, 60, and 64.

9. Claims 3-11, 14, 15, 22-25, 28-36, 40, 41, 58, and 62, are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kamb *et al.*, (US Patent No.6,060,240, filed on December 13, 1996).

Kamb *et al.*, teach the generation of beads comprising capture oligonucleotides or nucleic acids. Beads included commercially available nucleoside-derivatized CPG and polystyrene beads, e.g., available from Applied Biosystems, Foster City, Calif.; derivatized magnetic beads; polystyrene grafted with polyethylene glycol, e.g., TentaGel.TM., Rapp Polymerc, Tubingen Germany, and the like (column 10, third paragraph). Note that the beads used in this prior art are spherical in shape with a diameter ranging from 70 to 400 μm (column 21, fifth paragraph), Thus we can reasonablely approximate pores between beads in a column format to be the size of a bead equal to the diameter of the bead even through no exact porous size is available. Capture oligonucleotides could be attached to a bead for use (column 11, fourth paragraph). Various links might be employed: including hydrophilic links, such as polyethyleneoxy, saccharide, polyol, esters, amides, saturated or unsaturated alkyl, aryl, combinations thereof, and the like. Functionalities present on the bead may include hydroxy, carboxy, iminohalide, amino, thio, active halogen (Cl or Br), carbonyl, silyl, tosyl, mesylates, brosylates, triflates or the like (column 11, fifth and sixth paragraphs). The capture oligonucleotides could also be linked to the beads via a phosphodiester linkage to the phosphate of the 3'-terminal nucleotide via nucleophilic attack by a

hydroxyl (typically an alcohol) on the bead surface; or via a phosphoramidate linkage between the 3'-terminal nucleotide and a primary amine conjugated to the bead surface (column 12, fourth paragraph). The number of capture oligonucleotides that could be attached onto the surface of a 10 micron radius bead was about 3×10^{9} (~3.2×10^{14} probe per square centimeter). Note that the three-dimensional porous substrate of claims 4 and 28 has about 2×10^{-19} to 2×10^{-15} nmol/nm^2 of a capture polynucleotide which are equal to about 1.2×10^{10} to 1.2×10^{14} probe per square centimeter. As shown in Figure 7, 100 synthesis columns would produce one million different 24-mers. In a first series of couplings, one hundred (100) columns are used to synthesize one hundred (100) different 8-mers that remain attached to the beads in each column (column 15, second paragraph). Figure 11 and Example 10 (column 35) showed the hybridization of labeled cDNA with beads which were inside the column and contained different 24-mers.

Although Kamb *et al.*, did not describe: (1) the hybridization of one target nucleic acid to a capture polynucleotide; (2) a three-dimensional porous substrate wherein a porosity was in the range of about 25% to 80% (the space between two beads). In the absence of convincing evidence to the contrary the claimed invention, these limitations is considered as inherent to the reference taught by Kamb *et al.*. A column could be considered as a flow-through device.

Note that, although Kamb *et al.*, did not describe the limitation in claims 10, 24, 25, 34, and 36, the rejections were be made in view of the ambiguity of claims 10, 24, 25, 34, and 36.

10. Claims 44, 50-52, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beattie (US Patent No. 5,843,767, filed on April 10, 1996) over Dean *et al.*, (US Patent No. 5,843,662, filed on May 13, 1996).

The teachings of Beattie have been summarized previously, *supra.*

Beattie does not disclose a kit.

Dean *et al.*, did teach a kit for determining the concentration of nucleic acid.

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have organized: (1) a flow-through device as described in claims 1 and 60 and a house into which the flow-through device can be disposed into a kit; and (2) a three-dimensional porous substrate, a capture polynucleotide, and means for generating a capture polynucleotide into kits as described in claims 50-52 and 65 as suggested by Dean *et al.*. The kit format is utilized not only assemble a variety of different reagents together but ensure the quality and compatibility of the reagents. One having ordinary skill in the art would have been motivated to organize the method and components of Beattie's patent into a kit because a flow-through device for generating a target nucleic acid, a three-dimensional porous substrate and a related hybridization method were well known in the art at that time the inventions were made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these prior art together because all of these prior art are known and are easy to use.

11. Claims 50-52 and 65-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb *et al.*, (US Patent No. 6,060,240, filed on May 13, 1996) over Dean *et al.*, (US Patent No. 5,843,662, filed on May 13, 1996).

The teachings of Kamb *et al.*, have been summarized previously, *supra.*

Kamb *et al.*, does not disclose a kit.

Dean *et al.*, did teach a kit for determining the concentration of nucleic acid.

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have organized a three-dimensional porous substrate, a capture polynucleotide, and means for generating a capture polynucleotide into kits as described in claims 50-52 and 65-67 as suggested by Dean *et al.*. The kit format is utilized not only assemble a variety of different reagents together but ensure the quality and compatibility of the reagents. One having ordinary skill in the art would have been motivated to organize the method and components of Kamb *et al.*, into a kit because a flow-through device for generating a target nucleic acid, a three-dimensional porous substrate, and a related hybridization method were well known in the art at that time the inventions were made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these prior art together because all of these prior art are known and are easy to use.

Note that, although Kamb *et al.*, did not describe the limitation in claim 67, the rejection was be made in view of the ambiguity of claim 67.

Conclusion

12. Rejections found in the prior office action yet not restated herein above have been withdrawn.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu., Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
January 29, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

1/29/01